In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

CHRISTINA ANDERSON,	*	
	*	No. 20-830V
	*	Special Master Christian J. Moran
Petitioner,	*	
v.	*	
	*	Filed: November 1, 2024
SECRETARY OF HEALTH AND HUMAN SERVICES,	*	
	*	
Respondent.	*	

Leigh Finfer, Muller Brazil, LLP, Dresher, PA, for petitioner;
Andrew J. Henning and Neil Bhargava, United States Dep't of Justice, Washington, DC, for respondent.

DECISION DENYING COMPENSATION[1]

Christina Anderson alleges that an influenza ("flu") vaccine caused her to develop a rare neurologic condition, anti-NMDA receptor encephalitis.[2] She

[1] Because this Decision contains a reasoned explanation for the action taken in this case, it must be made publicly accessible and will be posted on the United States Court of Federal Claims' website, and/or at https://www.govinfo.gov/app/collection/uscourts/national/cofc, in accordance with the E-Government Act of 2002. 44 U.S.C. § 3501 note (2018) (Federal Management and Promotion of Electronic Government Services). This means the Decision will be available to anyone with access to the internet. In accordance with Vaccine Rule 18(b), the parties have 14 days to identify and move to redact medical or other information, the disclosure of which would constitute an unwarranted invasion of privacy. Any changes will appear in the document posted on the website.

[2] Christina Anderson's mother, Noelle Anderson, initiated the litigation by filing a petition on July 9, 2020 when Christina was still a minor. The caption was amended on October 7, 2024 after Christina reached the age of majority. In this Decision, "Ms. Anderson" refers to

retained an expert, Lawrence Steinman, to support her claim. The Secretary disputes Ms. Anderson's claim that the vaccines injured her and has, likewise, supported his position with reports from a neurologist the Secretary retained for this litigation, Eric Lancaster. Following the submission of these reports, the parties advocated through memoranda.

The parties dispute whether Ms. Anderson has anti-NMDA receptor encephalitis. However, this question does not need to be resolved, as Ms. Anderson has failed to show how a flu vaccine can cause anti-NMDA receptor encephalitis. Thus, she is not entitled to compensation.

I. Anti-NMDAR Encephalitis

Neurons contain receptors for N-methyl-D-aspartate, which contribute to the transmission of glutamate. Gleichman at 11082.[3] "The NMDAR has a complex three-dimensional shape. Part of the protein extends outside the cell to respond to neurotransmitters, while other parts are anchored in the cell membrane or inside the cell." Exhibit A (Dr. Lancaster's first report) at 7. The portions within the cell cannot bind with substances outside the cell. Instead, any binding between substances outside the cell must occur on the portion of the receptor that is also outside the cell. Id.

For reasons not understood, some people develop antibodies to a portion of the NMDA receptor. (Because these antibodies are directed against the host's tissue, they are sometimes known as "auto-antibodies.") The specific portion of NMDA receptor that is targeted is known as the GluN1 subunit. Exhibit A at 7.

When a person develops anti-NMDA receptor antibodies, the NMDA receptor does not work as intended. The person, consequently, develops anti-NMDA receptor encephalitis (sometimes referred to as "NMDAR encephalitis").

The presentation of anti-NMDA receptor encephalitis varies. According to Dr. Steinman, common symptoms include changes in behavior (such as paranoia,

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Christina Anderson, although most steps in the litigation were carried out by Noelle Anderson on her daughter's behalf.

[3] Amy J. Gleichman et al., Anti-NMDA Receptor Encephalitis Antibody Binding Is Dependent on Amino Acid Identity of a Small Region within the GluN1 Amino Terminal Domain, 32 J. NEUROSCIENCE 11082 (2012); filed as Exhibit A-5.

hallucinations, or aggressiveness), problems in cognition, memory deficits, speech disorders, and loss of consciousness. Exhibit 16 at 11 (citing University of Pennsylvania ("UPenn") website).[4] It appears that Dr. Lancaster generally concurs with this list. See Exhibit A at 6-8. Dr. Steinman and Dr. Lancaster agree that patients usually have mild symptoms but rapidly decline with more severe symptoms. Exhibit 16 at 11; Exhibit A at 7.

In addition to looking at symptoms, doctors will also consider the results of testing in considering whether a person suffers from anti-NMDA receptor encephalitis. Test results consistent with a diagnosis of anti-NMDA receptor encephalitis include abnormal EEGs and abnormalities in the cerebrospinal fluid. See Graus at 3.[5] Whether abnormalities are required for a diagnosis is disputed by Dr. Steinman and Dr. Lancaster. This point is discussed further in the section on diagnosis below. See Section VI.

II. Events in Ms. Anderson's Life[6]

A. Early History and Vaccination

Ms. Anderson was born in 2006. Exhibit 12 (affidavit) at ¶ 1. Before the vaccination, she did not have any health problems that are relevant to the question of whether the flu vaccination harmed her. See Resp't's Br. at 2. On September 4, 2017, when she was 11 years old, Ms. Anderson received the allegedly causal flu vaccine. Exhibit 1 at 2.

B. September 18, 2017 through September 22, 2017

Two weeks later, Ms. Anderson complained about a sore throat, nausea, headache, and a cough during an appointment at Texas Children's Pediatrics.

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[4] Dr. Steinman cites to reference 4b in his report, but the link to the UPenn Website is listed as reference 5a. See Exhibit 16 at 38 (citing https://www.med.upenn.edu/autoimmuneneurology/nmdar-encephalitis.html).

[5] Francesc Graus et al., A clinical approach to diagnosis of autoimmune encephalitis, 15 LANCET NEUROL. 391 (2016); filed as Exhibit A-6.

[6] For more detailed accounts of the medical records, see Pet'r's Br., filed Mar. 2, 2023, at 3-8 and Resp't's Br., filed June 1, 2023, at 2-10.

Exhibit 3 at 1-6 (Sep. 18, 2017). Dr. Tracie Butler diagnosed Ms. Anderson with a sore throat and an upper respiratory infection. Id. at 5-7.

Ms. Anderson was brought to the emergency department of Texas Children's Hospital the next day. Her complaints were similar--- generalized body pain, nausea, cough, and a headache. Exhibit 3 at 9-12. She was diagnosed with "[i]nfluenza due to unidentified influenza virus with other respiratory manifestations; [m]yalgia." Id. at 9.

Ms. Anderson was seen for a follow-up appointment at Texas Children's Pediatrics on September 20, 2017. The doctor wrote: "[Ms. Anderson] continues to have nausea intermittently and lower leg pain (mainly shins now). She can walk. Cough is dry." Exhibit 3 at 35. She tested negative for influenza A and influenza B. Id. at 30-36. The impression was "[m]yalgias probably viral vs[.] mild rhabdomyolysis?" Id. at 36.

The leg pain continued and Ms. Anderson was brought again to the emergency department at Texas Children's Hospital on September 21, 2017. Other complaints included weakness, nausea, abdominal pain, headache, itchiness, fatigue and lower back pain. Exhibit 3 at 41. She remained in the hospital overnight. A neurologic examination by a resident was normal. Exhibit 3 at 52. Ms. Anderson was discharged on September 22, 2017.

C. September 24, 2017 through September 28, 2017, including a Hospitalization[7]

A few days later, Ms. Anderson returned to Texas Children's Pediatrics. She reported headaches and body aches. Exhibit 3 at 211-19 (Sep. 25, 2017). The impression of the pediatrician, William Nix, was "severe headache and myalgias; I would bet that she has had some kind of viral encephalitis." Id. at 218. Dr. Nix recommended that Ms. Anderson consult a specialist in infectious diseases. Id.

A specialist in pediatric infectious diseases at Texas Children's Hospital, Ankhi Dutta, saw Ms. Anderson the same day. Exhibit 3 at 220-26 (Sep. 25, 2017). Ms. Anderson could not walk more than four or five steps. Id. at 226. Dr.

[7] Dr. Steinman estimates that Ms. Anderson began to manifest symptoms of her anti-NMDA receptor encephalitis around September 24, 2017. Exhibit 16 at 36; see also Pet'r's Br. at 27.

Dutta considered whether Ms. Anderson could be suffering from a post-viral syndrome and a demyelinating disease. Id. at 230. Dr. Dutta admitted Ms. Anderson to the hospital for various tests and a consult with neurology. Id. at 231.

In the hospital, a specialist in pediatric hospital medicine, Stephen Edwards, saw her. Exhibit 3 at 237-46. His differential diagnosis included "viral syndrome, encephalitis/meningitis, or migraine. Most likely diagnosis is viral syndrome . . . based on patient's age, history, exam and initial studies." Id. at 245. Dr. Edwards also recommended obtaining insights from a neurologist. Id. at 246.

After Dr. Edwards saw Ms. Anderson, blood was drawn. One result revealed a positive test for fluorescent antinuclear antibody ("FANA"). Exhibit 3 at 540.

Neurologist Edward Espineli saw Ms. Anderson roughly an hour after Dr. Edwards. Exhibit 3 at 246-54. Ms. Anderson was having headaches, generalized abdominal pain, leg pain, and joint pain. Id. at 247. Dr. Espineli did not identify any etiology immediately. He wanted to obtain results from various studies, including "autoimmune encephalitic labs." Id. at 253.

A lumbar puncture took place the next day. Exhibit 3 at 531. Dr. Espineli wrote: "The CSF was clean without signs of infection or inflammation. [Infectious Disease] is involved as well and agrees that an infectious etiology is not likely." Id. at 282.[8] More specifically, testing on the cerebrospinal fluid did not show any NMDA receptor antibodies. Exhibit 13 at 3-5. The normal results upset Ms. Anderson because she was worried "about not having an answer and not returning to her previously healthy status." Exhibit 3 at 280. Dr. Espineli prescribed Amitriptyline to help with her headaches, nerve pain, and sleep. Id. at 282. Dr. Espineli also noted that the Mayo Clinic serum autoimmune encephalitis panel remained pending. Id.

Dr. Espineli returned the next morning. Exhibit 3 at 301. The Amitriptyline helped Ms. Anderson to sleep. Id. Another medication, Solumedrol,

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[8] This decision does not identify the multiple types of tests that were conducted. As Dr. Espineli summarized: "The workup thus far has been unrevealing and it has been a very thorough workup. Inflammatory markers, infectious testing have all been normal." Exhibit 3 at 282.

resolved her pain. Id.; see also id. at 304. He anticipated seeing her about a week after she was discharged. Id. at 304.

At discharge, the diagnoses were myalgia and migraine with status migrainosus. Exhibit 3 at 306. Pdf 413. The discharging doctor anticipated that Ms. Anderson would see Dr. Nix and Dr. Espineli. Ms. Anderson also might see a rheumatologist.

D. Remainder of 2017

After leaving the hospital, Ms. Anderson saw a series of doctors on an outpatient basis. She first saw a pediatrician at Texas Children's Pediatrics, Anuradha McDonald, on October 2, 2017. Exhibit 3 at 488-91. Ms. Anderson was complaining about headaches, leg pain, back pain, nausea, and high blood pressure readings. She confided in Dr. McDonald that she has been feeling stressed with academics and softball. Id. at 488. Dr. McDonald recommended seeing a psychologist, consulting a cardiologist for her high blood pressure, maintaining the appointment with neurology, and possibly seeing an endocrinologist. Id. at 491.

An appointment with a rheumatologist, Amanda Brown, occurred on October 5, 2017, for "possible autoimmune disease and + ANA." Exhibit 3 at 508. Dr. Brown reviewed an extensive amount of laboratory studies. These generally "point[ed] away from a rheumatic disease." Id. at 541. She wrote that it was "interesting" that Ms. Anderson's "NMDA Ab serum is positive, CSF is pending." Id. (A copy of the results of the Mayo Clinic testing is found at Exhibit 8, page 3, but this document does not indicate when the results were reported). Dr. Brown considered whether Ms. Anderson might have autoimmune encephalitis and planned to discuss the case with "Dr. Muscal who specializes in AE [autoimmune encephalitis] cases." Exhibit 3 at 508.

The following day, Ms. Anderson returned to see Dr. Espineli, the neurologist who treated her during the hospitalization, on an out-patient basis. Exhibit 3 at 544. The main reason for the visit was dizziness. Id. Although Dr. Brown had stated that the NMDA results were positive, Dr. Espineli's record indicated that "Mayo Autoimmune Encephalitis panels CSF and Serum [were] pending." Id. at 553. Dr. Espineli continued the Amitriptyline. Id. at 563. He proposed that she might take Ondanestron because she was losing weight. He also concurred in the recommendations to see a psychologist and endocrinologist. Id.

Visits with an endocrinologist and cardiologist happened on October 17, 2017 and October 20, 2017, respectively. The evaluations regarding endocrinology and cardiology were generally normal. See Exhibit 3 at 592 (endocrinologist) and id. at 631 (cardiologist). However, both doctors referenced Ms. Anderson as suffering from autoimmune encephalitis. Id. at 591 ("most likely autoimmune type encephalitis") and at 631 ("presumed diagnosis of autoimmune encephalitis").

Ms. Anderson saw her neurologist, Dr. Espineli, on November 8, 2017. Exhibit 3 at 707-25. Dr. Espineli stated that Ms. Anderson had "autonomic dysfunction, so have started Florinef and referred her to see a Dysautonomia Specialist." Id. at 724. Pdf 831. "Dysautonomia" was the primary diagnosis. Another pertinent diagnosis was "Anti-NMDA receptor encephalitis." Id.

Eyal Muscal saw Ms. Anderson on December 5, 2017.[9] Exhibit 3 at 730-41. In the history Dr. Muscal obtained, Ms. Anderson recounted that she had been hearing noises and voices for years. Id. at 736. The history also states that "her NMDAR [antibody] was positive in serum but not CSF." Id. at 737. Ms. Anderson's mother brought a list of four conditions that she wished to explore with Dr. Muscal. Id.

Upon examination, Dr. Muscal identified that "cognition and memory are normal. She exhibits a depressed mood." Id. at 740. Dr. Muscal's impressions included several points, affecting the claim that the flu vaccination caused Ms. Anderson to suffer anti-NMDAR encephalitis. He stated that Ms. Anderson's "history and examination . . . does not seem [consistent] with autoimmune encephalitis phenotypes as per Grauss 2016 adult classification criteria. Additionally, she has no evidence of EEG, CSF or neurologic exam abnormalities." Id. at 741. Dr. Muscal also stated that Ms. Anderson's "dysautonomia cannot be easily unified with her other signs and symptoms." Id. Dr. Muscal was concerned that Ms. Anderson had been suffering from neuropsychological issues for years and planned to help her obtain neuropsychological evaluations. Id.

[9] Dr. Brown, as noted earlier, had identified him earlier as a specialist in autoimmune encephalitis. Exhibit 3 at 508.

Remaining appointments in 2017 concerned a gastroenterologist and cardiologist. These visits are not particularly relevant to determining whether Ms. Anderson suffered from anti-NMDA receptor encephalitis.

E. 2018

An initial psychiatric evaluation took place on January 30, 2018. Exhibit 3 at 1029-40. The chief complaint was depression due to a medical condition. Id. at 1035. Dr. Ashley Smith wrote that "some difficulty obtaining consistent history as to symptoms before recent illness" complicated Ms. Anderson's case. Id. at 1037. Part of the recent illness included testing positive for "anti NMDA in the blood but not spinal fluid." Id. at 1035. Dr. Smith diagnosed Ms. Anderson as suffering from "Depression and anxiety due to GMC, NMDA?" Id. at 1038.

Dr. Espineli saw Ms. Anderson on February 16, 2018. Exhibit 3 at 1063-103. The chief complaint was dysautonomia. Id. at 1082. Dr. Espineli memorialized challenges in determining what condition was affecting Ms. Anderson:

> Mother sent a MyChart message with several questions regarding her diagnosis. Mother is convinced that she has Limbic Encephalitis given her clinical symptoms and some of the lab findings. Rheumatology does not agree as the severity and range of symptoms are not consistent with the widely accepted classification criteria for this.[10] Dysautonomia Specialist also feels that certain autoimmune markers may be positive, but not indicative of a specific condition in patients with Dysautonomia. He has seen many patients who have random autoimmune markers positive, but no underlying condition aside from Dysautonomia found. Still, she has had a worsening of symptoms with orthostatic symptoms, abdominal pain, myalgias, difficulty concentrating, and short term memory issues.

Id. at 1084.

[10] The rheumatologist is probably Dr. Muscal.

Dr. Espineli's own diagnosis did not change, perhaps reflecting continuity in electronic medical records. He ordered a course of steroids. He also ordered more testing, including "Mayo Clinic Serum and CSF Paraneoplastic Autoimmune Encephalitis Panels." Id. at 1095; see also id. at 1069-70 (list of orders).

The results from the Mayo Clinic Medical Laboratories showed that Ms. Anderson's serum was positive for anti-NMDA receptor antibodies. Exhibit 8 at 4 (dated March 13, 2018); see also Exhibit 13 at 4. However, the panel on the cerebrospinal fluid was negative. Exhibit 13 at 11-20. Dr. Espineli commented on these results in an appointment on April 12, 2018.

Before Ms. Anderson saw Dr. Espineli, she saw her cardiologist, Dr. Burkholder, whom she had seen periodically for dizziness. Exhibit 6 at 5. Dr. Burkholder discussed a potential link to the vaccination: "The mother reports that many of these symptoms followed after a flu vaccine administration. There is literature that complex neurological disorders may occur post vaccination, Although it is impossible to prove at this time, it is certainly a possibility that the vaccination contributed to her neurological state seen today." Id. at 6. He recommended that Ms. Anderson increase her intake of fluids and implement techniques to cope with her stress. Id.

Due to "Dysautonomia/Encephalitis," Dr. Espineli saw Ms. Anderson on April 12, 2018. Exhibit 3 at 1369. He noted that the "Mayo Clinic Serum NMDA [was] positive again [and] CSF negative again." Id. at 1377. He also referred to "MyChart emails and telephone notes regarding the positive serum NMDA, but negative CSF NMDA."[11] Id. Dr. Espineli added that "Mayo thinks this is false positive." Id. at 1381.

Dr. Espineli's summary is worth recounting in full, as he comments on the potential diagnosis of NMDA encephalitis and a potential cause for her illness:

> To summarize, it appears early on, she had some post-infectious/autoimmune issue (Unknown etiology - flu?) that left her with autonomic dysfunction, behavioral changes. She has been improving with time, but also after course of steroids. Whether this was an atypical NMDA

[11] These materials have not been filed. See Resp't's Rep. at 8 n.3.

> autoimmune encephalitis or just Dysautonomia, IVIG can be helpful, so [we] will move forward with monthly treatments and reassess.

Id. at 1387.

About one month later, Dr. Espineli saw Ms. Anderson in follow up. Unlike other appointments, the chief complaint was "Anti-NMDA Receptor Encephalitis." Exhibit 3 at 1472 (May 9, 2018). He recounted that after the last visit, Ms. Anderson "did get IVIG, but not the entire amount." Id. at 1474. "She is doing much better. She feels that she is almost 100% - maybe 95%. Her depression has improved – smiling appropriately more. No pains noted." Id. Dr. Espineli seemed to support a plan in which Ms. Anderson would see other specialists less frequently. Id. at 1484. He wrote that Ms. Anderson's course "is pointing to an atypical form of NMDA Encephalitis." Id.

Over the next few months, Ms. Anderson had some relatively minor medical issues that resolved quickly. These medical records do not affect whether she suffered from anti-NMDA receptor encephalitis.

A more relevant medical record memorializes Ms. Anderson's next appointment with Dr. Espineli, which was on August 3, 2018. Exhibit 3 at 1637-49. She was generally much improved. "No further depression and is no longer seeing a Psychiatrist. The abdominal pain has resolved. No further headaches." Id. at 1639. On the other hand, she still had problems with focusing and memory. Ms. Anderson's mother asked whether another round of IVIG would be beneficial. Id. Dr. Espineli planned to explore repeating the IVIG treatment, despite Ms. Anderson's reaction to the first dose of IVIG. Dr. Espineli planned to consult Dr. Muscal, the rheumatologist, who has been "integral" in caring for Ms. Anderson Id. at 1649. Before determining whether to proceed with IVIG, Dr. Espineli wanted to obtain results from neuropsychological testing and to discuss the situation with Dr. Muscal. Id.[12]

[12] In an exchange of emails in later August, Ms. Anderson's mother and Dr. Espineli commented on how Ms. Anderson "did turn the corner with IVIG." Exhibit 10 at 26. In this context, Ms. Anderson's mother lamented that Dr. Muscal did not follow through and wondered whether if her daughter would be healthier if she had received IVIG earlier. Id.

Neuropsychological testing was conducted on August 6, 2018. She showed "numerous strengths." Exhibit 9 at 11. A relative weakness was difficulty with attention. The neuropsychologist commented: "Although [Ms. Anderson's] medical diagnosis has been challenging for her physicians to pinpoint, ongoing difficulties with attention are certainly not uncommon in individuals who have experienced inflammation within the brain (e.g., encephalitis) or other neurological conditions." Id.

The reports from the neuropsychologist were reviewed in a November 5, 2018 appointment with Dr. Espineli. Exhibit 10 at 41. Ms. Anderson was doing well and had no concerns. Id. at 33. She was not seeing any other specialists. Id. at 49. He again ordered testing through the Mayo Clinic. Id. at 49; see also id. at 38-39 (orders).[13] Dr. Espineli planned to see her in three months. Id. at 50.

It appears that some mistake occurred in the transmission of Ms. Anderson's bloodwork. A different laboratory, ARUP, tested Ms. Anderson's blood for NMDA receptor antibodies and the results were negative. Exhibit 10 at 38-39; see also Exhibit 10 at 74-75 (emails from Ms. Anderson's mother).[14] When this discrepancy was discovered, the Mayo Clinic had sufficient blood to perform additional testing. Id. at 80.

The Mayo Clinic's test of serum was negative for NMDA receptor antibodies. Exhibit 13 at 25-29. Both Ms. Anderson's mother and Dr. Espineli were very excited by this result. Exhibit 10 at 85.

The parties did not extensively discuss any more recent medical records. See Pet't's Br. at 8; Resp't's Br. at 10.

III. Procedural History

The procedural history is straightforward. Represented by Ms. Finfer, Ms. Anderson's mother started this case by alleging the flu vaccine caused Ms.

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[13] Dr. Espineli ordered testing on Ms. Anderson's blood, not her cerebrospinal fluid because Dr. Espineli thought that the CSF would not suddenly become positive. Exhibit 10 at 60 (email exchange with Ms. Anderson's mother).

[14] The Mayo Clinic actually ran a paraneoplastic panel. Exhibit 10 at 80. The results showed some non-significant results. Id.

Anderson to develop anti-NMDA encephalitis. Pet., filed July 9, 2020, ¶ 47. She periodically submitted medical records and affidavits.

The Secretary opposed the claim for compensation. Resp't's Rep., filed Dec. 14, 2020. The Secretary noted that Ms. Anderson had not presented a report from a treating doctor or from a retained expert that causally connected the vaccinations to Ms. Anderson's condition. Id. at 10-11.

To facilitate the presentation of reports from experts, a set of instructions were proposed. When the parties did not object, the instructions became final. Order, issued Jan. 12, 2021.

The parties submitted a series of reports from experts. As mentioned, Ms. Anderson retained Dr. Steinman. Special masters are familiar with Dr. Steinman as he frequently presents opinions supporting claims for compensation. Dr. Steinman is a board-certified neurologist. Exhibit 17 (curriculum vitae). Since 1980, he has taught at Stanford University in various roles, including professor. At the time of his first report, he had written more than five hundred articles published in peer-reviewed journals. Id. However, none of the articles appear to address anti-NMDA receptor encephalitis. In his first report, Dr. Steinman did not directly answer a question about how many patients with NMDA receptor encephalitis he has treated for this condition. Exhibit 16 at 3.

The Secretary's expert is Dr. Lancaster. Dr. Lancaster is board-certified in neurology. Exhibit C (curriculum vitae). He has "expertise in antibody-mediated neurologic disorders." Id. at 1. Dr. Lancaster has written more than 30 peer-reviewed articles, some of which concern anti-NMDA receptor encephalitis. Exhibit C at 5-7. In his first report, Dr. Lancaster did not specify the number of patients whom he has treated for NMDA receptor encephalitis. Exhibit A at 1.

Across the series of reports, Dr. Steinman and Dr. Lancaster disputed at least two aspects of the case: first, whether Ms. Anderson suffers from anti-NMDA receptor encephalitis, and second, whether there is a reputable theory by which the flu vaccine can cause anti-NMDA receptor encephalitis. See Exhibit 16 (Dr. Steinman's first report, dated Oct. 23, 2021); Exhibit A (Dr. Lancaster's first report, dated Mar. 6, 2022); Exhibit 18 (Dr. Steinman's second report, dated July 13, 2022); and Exhibit B (Dr. Lancaster's second report, dated Oct. 11, 2022). As to the theory, Dr. Steinman proposed molecular mimicry. However, Dr. Lancaster questioned how molecular mimicry can explain the development of anti-NMDA

receptor encephalitis. These reports are summarized in more detail in the analysis section.

The submission of Dr. Lancaster's second report appeared to complete the disclosure of reports from experts. Thus, the parties were directed to file briefs. Order, issued Dec. 16, 2022. This order alerted the parties that the case might be resolved on the papers. Ms. Anderson filed her primary brief on Mar. 2, 2022. The Secretary submitted his brief on June 1, 2023, and a corrected version of the brief on June 17, 2024.

Ms. Anderson further argued her case. Pet'r's Reply, filed July 3, 2023. With the submission of the reply, Ms. Anderson's case is ready for adjudication.

Ms. Anderson did not seek a hearing. See Pet'r's Br. The Secretary maintained that a hearing would be a waste of resources. Resp't's Br. at 19. Because both parties have had a fair opportunity to present their evidence and their arguments, an adjudication based upon the papers is appropriate. See Kreizenbeck v. Sec'y of Health & Hum. Servs., 945 F.3d 1362, 1365 (Fed. Cir. 2018).

IV. Standards for Adjudication

A petitioner is required to establish her case by a preponderance of the evidence. 42 U.S.C. § 300aa–13(1)(a). The preponderance of the evidence standard requires a "trier of fact to believe that the existence of a fact is more probable than its nonexistence before [he] may find in favor of the party who has the burden to persuade the judge of the fact's existence." Moberly v. Sec'y of Health & Hum. Servs., 592 F.3d 1315, 1322 n.2 (Fed. Cir. 2010) (citations omitted). Proof of medical certainty is not required. Bunting v. Sec'y of Health & Hum. Servs., 931 F.2d 867, 873 (Fed. Cir. 1991).

Distinguishing between "preponderant evidence" and "medical certainty" is important because a special master should not impose an evidentiary burden that is too high. Andreu v. Sec'y of Health & Hum. Servs., 569 F.3d 1367, 1379-80 (Fed. Cir. 2009) (reversing special master's decision that petitioners were not entitled to compensation); see also Lampe v. Sec'y of Health & Hum. Servs., 219 F.3d 1357 (Fed. Cir. 2000); Hodges v. Sec'y of Health & Hum. Servs., 9 F.3d 958, 961 (Fed. Cir. 1993) (disagreeing with dissenting judge's contention that the special master confused preponderance of the evidence with medical certainty).

These standards for adjudication are the foundation for the analysis, which is set out in three parts below. The first part of the analysis finds that Dr. Lancaster is better qualified to discuss anti-NMDA receptor encephalitis. This finding, in turn, contributes to the subsequent two parts of the analysis. In the next part, Ms. Anderson has not established that anti-NMDA receptor encephalitis is appropriate diagnosis. The final part finds that Ms. Anderson has not established all elements of a causation-in-fact claim.

V. Analysis Part One: Qualifications of Experts

Special masters may consider the relative expertise of testifying experts when weighing the value of their opinion. See Depena v. Sec'y of Health & Hum. Servs., No. 13-675V, 2017 WL 1075101 (Fed. Cl. Spec. Mstr. Feb. 22, 2017), mot. for rev. denied, 133 Fed. Cl. 535, 547-48 (2017), aff'd without op., 730 Fed. App'x 938 (Fed. Cir. 2018); Copenhaver v. Sec'y of Health & Hum. Servs., No. 13-1002V, 2016 WL 3456436 (Fed. Cl. Spec. Mstr. May 31, 2016), mot. for rev. denied, 129 Fed. Cl. 176 (2016).

On the topic of anti-NMDA receptor encephalitis, Dr. Lancaster's qualifications *greatly* outweigh Dr. Steinman's qualifications. Dr. Lancaster worked with Dr. Joseph Dalmau, who discovered anti-NMDA receptor encephalitis. See Exhibit A-3 (Dalmau)[15] (including Dr. Lancaster as a contributing author). With Dr. Dalmau, Dr. Lancaster has co-authored 15 articles, published in peer-reviewed journals, about anti-NMDA receptor encephalitis. Exhibit C at 4-6. Dr. Lancaster also routinely diagnoses and treats patients with this disease. Exhibit A at 1.

In contrast, Dr. Steinman does not have this same focus on anti-NMDA receptor encephalitis. Dr. Steinman's work has generally focused on demyelinating illnesses, such as multiple sclerosis.

Accordingly, Dr. Lancaster is better qualified to discuss anti-NMDA receptor encephalitis based upon his training, research, and experience. The strength of Dr. Lancaster's opinion and the corresponding relative weakness of Dr.

[15] J. Dalmau et al., Clinical experience and laboratory investigations in patients with anti-NMDAR encephalitis, 10 LANCET NEURO 63 (2011); filed as Exhibit A-3.

Steinman's competing opinion underlie much of the analysis in the following sections.[16]

VI. Analysis Part Two: Diagnosis

In Broekelschen v. Sec'y of Health and Hum. Servs., 618 F.3d 1339, 1346 (Fed. Cir. 2010), the Federal Circuit recognized that in some circumstances, the special master may "first determine which injury was best supported by the evidence in the record before applying the Althen test." See also Lombardi v. Sec'y of Health & Hum. Servs., 656 F.3d 1343, 1352-53 (Fed. Cir. 2011) (finding that "it was appropriate for the special master to first determine what injury, if any, was supported by the evidence presented in the record before applying the Althen test to determine causation" when there was disagreement among experts about diagnosis); Hibbard v. Sec'y of Health & Hum. Servs., 698 F.3d 1355, 1368 (Fed. Cir. 2012) (special master was not arbitrary and capricious in reviewing the evidence and determining that petitioner did not have injury she alleged where there was an "array of different opinions among [the petitioner's] examining and treating physicians as to the cause or causes of her symptoms"). Here, through their experts, the parties dispute whether Ms. Anderson suffered from anti-NMDA receptor encephalitis. See Pet'r's Br. at 11-17; Resp't's Corrected Br. at 12-14; Pet'r's Reply at 1-4. The evidence does not preponderate in Ms. Anderson's favor.

A basic reason for finding that Ms. Anderson has not established the diagnosis of anti-NMDA receptor encephalitis is that Dr. Lancaster disagrees with it. As explained in the Section V. above, Dr. Lancaster has more experience with this disease than Dr. Steinman. Thus, it seems to make sense to give greater credence to the more knowledgeable person.

A more complicated reason is that Ms. Anderson does not fulfill the diagnostic criteria for anti-NMDA receptor encephalitis. Dr. Lancaster put

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[16] The Secretary also questions Dr. Steinman's credibility as an expert witness by citing statements from special masters. See Resp't's Corrected Br. at 21. Dr. Steinman's history of opining in favor of petitioners in the Vaccine Program does not contribute to the outcome of this case.

Nevertheless, Dr. Steinman appears to have stretched to an area in which he lacks his usual degree of expertise. Whether the amount of compensation for Dr. Steinman should be reduced will depend, in part, upon whether the Secretary objects to the amount of compensation. See Vaccine Rule 13(a)(3).

forward the Graus criteria. Exhibit A at 9, citing Graus.[17] Special masters have accepted this source. See Phelan v. Sec'y of Health & Hum. Servs., No. 18-1366V, 2024 WL 1174097, at *34 (Fed. Cl. Spec. Mstr. Feb. 20, 2024); Moriarty v. Sec'y of Health & Hum. Servs., No. 03-2876V, 2016 WL 5390172, at *28-31 (Fed. Cl. Spec. Mstr. Aug. 23, 2016), mot. for rev. granted, 130 Fed. Cl. 573 (2017).

One factor in the Graus criteria is whether the person's cerebrospinal fluid ("CSF") contains "pleocytosis or oligoclonal bands." Graus at 7 (panel 4, item 2). Ms. Anderson cerebrospinal fluid was negative. Exhibit 13 at 3-5; see also Exhibit A at 3. This normal result is one reason that Dr. Lancaster rejects the diagnosis of anti-NMDA receptor encephalitis. Exhibit A at 8-9.

However, Dr. Steinman points to the detection of antibodies in Ms. Anderson's serum. Exhibit 16 at 12, citing the UPenn website. As discussed in the recitation of Ms. Anderson's medical records, the doctors who treated her were also puzzled by the discrepancy between the CSF test and the serum test. See, e.g., Exhibit 3 at 1381 (note that Mayo Clinic believed the serum test was a false positive).

Ultimately, Dr. Lancaster's explanation about why the cerebrospinal fluid test is more important is persuasive.[18] Dr. Lancaster stated that information in the UPenn website, which he either authored or co-authored, is intended for a general audience, not medical professionals. Exhibit E at 1. Dr. Lancaster also said that in

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[17] Francesc Graus, et al., A clinical approach to diagnosis of autoimmune encephalitis, 15 LANCET NEUROL 391 (2016); filed as Exhibit A-6. Dr. Lancaster is one of the authors of this position paper.

[18] Due to procedural irregularities, Dr. Lancaster's response was delayed. Dr. Steinman's first report explicitly listed the UPenn website and he included it among his references. Exhibit 16 at 12 & 38 (item 5a). However, counsel did not file the UPenn website or any of the other articles Dr. Steinman had cited. See CM/ECF No. 31.

When Dr. Lancaster addressed Dr. Steinman's first report, Dr. Lancaster did not discuss the UPenn website. See Exhibit A. When this omission was identified, the Secretary was directed to have Dr. Lancaster present his opinion. Order, issued Apr. 19, 2024. Dr. Lancaster did so. Exhibit E. In the June 5, 2024 status conference, Ms. Anderson declined to seek another report from Dr. Steinman. Order, issued June 5, 2024; see also Pet'r's Status Rep., filed July 1, 2024 (declining to file a reply brief in response to the Secretary's corrected brief).

his practice, he references the Graus criteria. Id. at 2. This discussion is credited as persuasive.

Accordingly, Ms. Anderson has not demonstrated with preponderant evidence that anti-NMDA receptor encephalitis is an appropriate diagnosis. Without this showing, she cannot receive compensation.

VII. Analysis Part Three: Causation-in-Fact

Assuming that Ms. Anderson had established her diagnosis, then to receive compensation she must establish that the vaccine was the cause-in-fact of the anti-NMDA receptor encephalitis. When a petitioner, like Ms. Anderson, claims that a vaccine caused an injury not listed on the Vaccine Injury Table, such as anti-NMDA receptor encephalitis, the elements of a petitioner's case are well defined. A petitioner bears a burden "to show by preponderant evidence that the vaccination brought about [the vaccinee's] injury by providing: (1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of a proximate temporal relationship between vaccination and injury." Althen v. Sec'y of Health & Hum. Servs., 418 F.3d 1274, 1278 (Fed. Cir. 2005).

In this case, the critical element is prong one.

A. Prong One --- Theory Dr. Steinman Advances

Ms. Anderson advances the theory of molecular mimicry. Pet'r's Br. at 18-21.

1. Appellate Cases regarding Molecular Mimicry

Because special masters are often called upon to evaluate the persuasiveness of the theory of molecular mimicry, the Court of Federal Claims and the Court of Appeals for the Federal Circuit have considered molecular mimicry in their appellate role of reviewing opinions.[19] In December 2019, the undersigned identified the leading precedents as W.C. v. Sec'y of Health & Hum. Servs., 704 F.3d 1352 (Fed. Cir. 2013), and Caves v. Sec'y of Dep't. of Health & Hum. Servs.,

[19] The briefs would have been improved if they had discussed any appellate cases about molecular mimicry.

100 Fed. Cl. 119 (2011), aff'd sub nom., 463 F. App'x 932 (Fed. Cir. 2012). Tullio v. Sec'y of Health & Hum. Servs., No. 15-51V, 2019 WL 7580149, at *12-14 (Fed. Cl. Spec. Mstr. Dec. 19, 2019), mot. for rev. denied, 149 Fed. Cl. 448 (2020). While Tullio describes those cases in more detail, their essence appears to be that although molecular mimicry is accepted in some contexts, special masters may properly require some empirical evidence to show that a particular vaccine can cause a particular disease.

In the next approximately four years, appellate authorities reviewing decisions involving molecular mimicry have generally endorsed the approach of looking for some evidence that persuasively shows that a portion of a vaccine resembles a portion of human tissue, which contributes to causing the disease, and that the immune system will respond to the relevant amino acid sequence.[20] Chronologically, the list of more recent appellate cases begins with the opinion in Tullio, which denied the motion for review. 149 Fed. Cl. 448, 467-68 (2020).

Another example in which the Court of Federal Claims held that the special master did not elevate the petitioner's burden of proof in the context of evaluating the theory of molecular mimicry is Morgan v. Sec'y of Health & Hum. Servs., 148 Fed. Cl. 454, 476-77 (2020), aff'd in non-precedential opinion, 850 F. App'x 775 (Fed. Cir. 2021). In Morgan, the Chief Special Master found that petitioner had not presented persuasive evidence about a relevant antibody. Id. at 477. The Chief Special Master also noted that the articles about the relevant disease do not list the wild flu virus as potentially causing the disease. Id. When examining this analysis, the Court of Federal Claims concluded: "the Chief Special Master did not raise the burden of causation in this case; petitioner simply failed to meet it." Id.

The Federal Circuit also evaluated the Chief Special Master's approach in Morgan. The Federal Circuit concluded: "We discern no error in the special master's causation analysis." 850 F. App'x 775, 784 (Fed. Cir. 2021).

Most other recent appellate cases follow this path. See, e.g., Stricker v. Sec'y of Health & Hum. Servs., 170 Fed. Cl. 701, 720-21 (2024); Duncan v. Sec'y of Health & Hum. Servs., 153 Fed. Cl. 642, 661 (2021) (finding the special master

[20] The term "homology" is used when discussing molecular mimicry. "Homology" is defined as "the quality of being homologous; the morphological identity of corresponding parts; structural similarity due to descent from a common form." *Dorland's* at 868.

did not err in rejecting a bare assertion of molecular mimicry and stating "there is an important difference between the general theory of molecular mimicry and the more specific theory that the vaccine at issue is capable of triggering an autoimmune response that culminates in the petitioner's injury"); Caredio v. Sec'y of Health & Hum. Servs., No. 17-79V, 2021 WL 6058835, at *11 (Fed. Cl. Dec. 3, 2021) (indicating that a special master did not err in requiring more than homology and citing Tullio); Yalacki v. Sec'y of Health & Hum. Servs., 146 Fed. Cl. 80, 91-92 (2019) (ruling that special master did not err in looking for reliable evidence to support molecular mimicry as a theory); but see Patton v. Sec'y of Health & Hum. Servs., 157 Fed. Cl. 159, 169 (2021) (finding that a special master erred in requiring petitioner submit a study to establish medical theory causally connecting flu vaccine to brachial neuritis).

The Court of Federal Claims explained why petitioners must present some evidence to show the persuasiveness of molecular mimicry as a theory in their cases. Dennington v. Sec'y of Health & Hum. Servs., 167 Fed. Cl. 640 (2023), appeal withdrawn, No. 2024-1214 (Fed. Cir. Mar. 25, 2024). There, Ms. Dennington alleged that a tetanus-diphtheria-acellular pertussis ("Tdap") vaccine caused her to develop GBS. Id. at 644. She supported her claim with two reports from a neurologist, Carlo Tornatore, who put forward molecular mimicry. Id. at 647-49. The chief special master denied entitlement. Id. at 656.

The Court of Federal Claims denied a motion for review because the Chief Special Master did not commit any error in evaluating Ms. Dennington's prong one evidence. The Court emphasized the lack of evidence supporting Dr. Tornatore's opinion:

- "While Petitioner and Dr. Tornatore put forth the well-established medical theory of molecular mimicry as the mechanism through which the Tdap vaccine could cause GBS, nowhere in Dr. Tornatore's expert reports, nor in Petitioner's briefs, do they specifically tie the Tdap vaccine to GBS through molecular mimicry." Id. at 653.

- "Dr. Tornatore never actually explains how molecular mimicry might occur from the Tdap vaccine specifically, nor does he elaborate on how molecular mimicry could cause the specific autoimmune system reaction that could cause GBS." Id.

- "There is nothing in Dr. Tornatore's report that explains or even alludes to what antigens or structures in the Tdap vaccine could share homology with possible host antigens and how these antigens could react in the manner GBS is believed to progress." Id. at 654.

- "The literature upon which he relies make no mention of any causal connection between GBS and the Tdap vaccine." Id.

Based upon these observations, the Court criticized the lack of specificity in Dr. Tornatore's opinions:

> In fact, because Dr. Tornatore does not offer any specific explanation as to the distinct connection between Tdap, molecular mimicry, and GBS, one could take Dr. Tornatore's causation theory and substitute any table vaccine (e.g., the measles vaccine) and any autoimmune disorder (e.g., autoimmune encephalitis) and Dr. Tornatore's expert report's discussion of molecular mimicry would require absolutely no changes. That is how general her molecular mimicry theory is—it does not matter which vaccine and which autoimmune disorder are plugged in. But *Althen* prong one requires more.

Id.

In accordance with precedents such as W.C., Caves, Tulio, Yalacki, Stricker, Duncan, and Dennington, the undersigned will look to see whether any evidence supports the theory that flu vaccine can cause anti-NMDA receptor encephalitis.

2. Evidence regarding Molecular Mimicry

Molecular mimicry is a theory to explain how a person's immune system might malfunction. Normally, the immune system protects people against foreign invaders, such as bacteria and viruses. To simplify, the immune system consists of two arms: the innate immune system and the adaptive immune system. The initial response comes from the innate immune system. When the innate immune system fails to resolve the threat posed by the foreign invader, the adaptive immune system starts. The adaptive immune system, in turn, involves both T cells and B cells. T cells and B cells eradicate different invaders differently.

The theory of molecular mimicry posits that some foreign invaders resemble (or mimic) human tissue. Thus, when the body's immune system responds to the foreign substance, the immune system inadvertently attacks the host's tissue. Dr. Steinman has frequently offered this theory in supporting claims that a vaccination harmed someone.

Here, the Secretary disputes the persuasiveness of Dr. Steinman's opinion that the flu vaccine can cause NMDAR-encephalitis. Resp't's Corrected Br. at 14-18. Contested aspects include (a) whether molecular mimicry can explain how a disease based on B cells develop, (b) whether a similarity in sequences of amino acids is common or rare, and (c) the usefulness of a database listing epitopes.

a) Molecular Mimicry and B Cells

Dr. Steinman disclosed his opinion about molecular mimicry in his first report. Exhibit 16 at 16-35. Dr. Steinman states that "Patients with NMDA encephalitis have antibodies bind to epitopes located at the amino terminal domain (ATD) of the GluN1 receptor." Id. at 16. He explains that NMDAR encephalitis is a coordinated T cell and B cell mediated immune response. The T cell initiates the B cell response, which he describes as "basic immunology." Id. at 17. A fairly substantial portion of Dr. Steinman's report concerns how T cells activate B cells. Id. at 16-24. "To summarize, NMDA-R encephalitis results from a concerted pathophysiology mediated by T helper cells and B cells producing NMDA-R antibody." Id. at 24.

Dr. Steinman then explains that shared structures in a vaccine can trigger a cross-reactive response to the self. An autoimmune disease occurs when there is cross-reaction between the virus and the host at a "disease-related" epitope. Id. at 24-26.

Dr. Steinman discussed whether there are homologies between the NMDA receptor (which is targeted in NMDAR encephalitis) and components of the flu vaccine Ms. Anderson received. Exhibit 16 at 26-27. He noted that "a viral peptide with homology at just 5 amino acids within a stretch of 12 amino acids can induce clinical signs of encephalitis [within] the classic experimental autoimmune encephalomyelitis model." Id. at 27. The five amino acids do not have to be consecutive. Id. Using BLAST searches, Dr. Steinman identified a sequence with 6 identical amino acids, containing a peptide that is a mimic of the NMDA receptor. Id. at 34. Thus, he concluded, "There is a component of the 2017-2018

influenza vaccine that COULD cause NMDA receptor encephalitis in a susceptible individual." Id. at 35.

Dr. Lancaster found Dr. Steinman's explanation inadequate. Dr. Lancaster stated that the antibodies that attack the NMDA receptor cause the encephalitis. Exhibit A at 10. "Any autoimmune mechanism based upon molecular mimicry must therefore account for the generation of these specific antibodies." Id. He states that although B cells and T cells interact to generate immune responses, "the mere activation of T cells is not sufficient to cause these precise antibodies," and "no component of a vaccine . . . has any sufficient homology to be likely to generate the relevant antibody response." Id. In Dr. Lancaster's view, "Dr. Steinman's theory is deficient and unreliable because it sidesteps the issue of how such precise antibodies would be generated in order to only discuss T cell responses." Id.

Further, Dr. Lancaster stated that "Short stretches of amino acid homology are not reliable predictors of clinically relevant molecular mimicry," and that the scientific community generally agrees "that short stretches of amino acid homology up to 8 in a row are not significant." Exhibit A at 10. Dr. Lancaster opined that homology of the degree found by Dr. Steinman is "not a rare of special occurrence but rather mundane and uninformative about predicting autoimmunity," noting that Dr. Steinman previously used BLAST searches to identify similar homologies in the Rubella and Mumps viruses in arguing that they could cause anti-NMDAR encephalitis. Id. at 11.

Based on Dr. Lancaster's opinion, the Secretary argues that Dr. Steinman "fails to address the crux of the issue: the theory of molecular mimicry is predicated on *T cells directly attacking self-tissues*, which is not part of the pathophysiology of anti-NMDAR encephalitis and does not extend to the production of antibodies." Resp't's Corrected Br. at 18 (emphasis added).

Special masters have encountered this issue without really resolving it. See K.A. v. Sec'y of Health & Hum. Servs., No. 16-989V, 2022 WL 20213037, at *10 n.7 (Fed. Cl. Spec. Mstr. Apr. 18, 2022), mot. for rev. denied, 164 Fed. Cl. 98 (2022), aff'd, 2024 WL 2012526 (Fed. Cir. May 7, 2024); L.C. v. Sec'y of Health & Hum. Servs., No. 17-722V, 2021 WL 3630315, at *8 n.7 (Fed. Cl. Spec. Mstr. June 2, 2021); Abbott v. Sec'y of Health & Hum. Servs., No. 99-497V, 2010 WL 3186269, at *12-18 (Fed. Cl. Spec. Mstr. June 28, 2010) (finding that molecular mimicry cannot explain a B cell-based disease in an infant six months old). Special masters have recited evidence from other cases showing that molecular

mimicry can involve T cells and B cells. See, e.g. Farag v. Sec'y of Health & Hum. Servs., No. 17-714V, 2023 WL 7203034, * 16 (Fed. Cl. Spec. Mstr. Sep. 29, 2023) (quoting respondent's expert as stating "the two arms of the immune system that are implicated in autoimmunity, potentially through molecular mimicry, are B cells and T cells").

In Ms. Anderson's case, the written record does not permit a clear answer to this question. Although Dr. Steinman responded to Dr. Lancaster's first report, Dr. Steinman did not address the question of T cells versus B cells. See Exhibit 18. Similarly, Ms. Anderson did not turn to this point after the Secretary's argument. See Pet'r's Reply. Thus, some questions about whether molecular mimicry can explain a disease based on B cells remain unaddressed.

Given the amount of indeterminacy, the better course is not to make any finding regarding molecular mimicry and diseases based on B cells. As discussed in the following sections, the Secretary has raised other points, which undermine the persuasiveness of Dr. Steinman's opinion. Thus, even if Ms. Anderson were found to have established that molecular mimicry can lead to the generation of autoantibodies, she still would not be credited with meeting her burden on prong one.

b) Commonness of Homologous Stretches of Amino Acids

In creating an opinion that the flu vaccine can cause anti-NMDA receptor encephalitis, Dr. Steinman queried two databases. The first is the Basic Local Alignment Search Tool ("BLAST"). The second is the immune epitope database, which is discussed in section c, below.

Dr. Steinman's consultation of BLAST contains two parts: a query of the database and then a filtration of results, looking for sequences of amino acids in which 5 out of 12 amino acids were the same. See Exhibit 16 at 27-33; see also Pet'r's Br. at 20. Dr. Steinman stated that a standard of 5 out of 12 could yield meaningful results, based on the findings of three papers, collectively known as the Gautum articles.[21] Exhibit 16 at 27-33; see also Resp't's Corrected Br. at 16 (summarizing Dr. Steinman's opinion).

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[21] A.M. Gautam et al., A polyalanine peptide containing only five native myelin basic protein residues induces autoimmune encephalomyelitis, 176 J. EXP. MED. 605 (1992); filed as Exhibit 16(10).

An obstacle to finding Dr. Steinman's opinion persuasive is Dr. Lancaster's opinion that the "general consensus of the scientific community is that short stretches of amino acid homology up to 8 in a row are not significant." Exhibit A at 10. These short sequences of identical amino acids are not meaningful because "there are only 20 amino acids." Id. "Finding homology to this degree is therefore not a rare or special occurrence but rather mundane and uninformative about predicting autoimmunity." Id. at 11. To support his opinion, Dr. Lancaster relied, in part, on an article by Silvanovich.[22] Dr. Steinman did not negate this portion of Dr. Lancaster's opinion. See Exhibit 18.[23]

The BLAST searches, therefore, do not meaningfully advance Dr. Steinman's assertion of molecular mimicry. As discussed in Silvanovich, identifying sequences of amino acids that satisfy the 5 out of 12 standard is relatively easy. Although Dr. Steinman seems to portray an identified homology between a flu vaccine and NMDA receptor as something strikingly unusual (and, therefore, potentially causative), the homology is actually much more routine. The results of the Gautum experiments show that sometimes some homologous regions produce cross-reactions. However, the Gautum experiments also show that a cross-reaction does not always happen simply when 5 out of 12 amino acids are the same. See Sparrow v. Sec'y of Health & Hum. Servs., No. 18-295V, 2024 WL 1599165 at *24-25 (Fed. Cl. Spec. Mstr. Mar. 19, 2024), mot. for rev. denied, 2024 WL 4353534 (Sept. 11, 2024).

For flu vaccine – NMDAR receptor, Dr. Steinman has not provided a persuasive basis for finding that what might occur is likely to occur. See Cedillo v.

A.M. Gautam et al., Minimum structural requirements for peptide presentation by major histocompatibility complex class II molecules: Implications in induction of autoimmunity, 91 PROC. NATL. ACAD. SCI. USA 767 (1994); filed as Exhibit 16(11).

A.M. Gautam et al., A viral peptide with limited homology to a self-peptide can induce clinical signs of experimental autoimmune encephalomyelitis, 161 J. IMMUNOL. 60 (1998); filed as Exhibit 16(12).

[22] A. Silvanovich et al., The value of short amino acid sequence matches for prediction of protein allergenicity, 9 TOXICOL. SCI. 252 (2006); filed as Exhibit A-10.

[23] The portion of Dr. Steinman's second report that defends his theory is mostly about how the Epstein-Barr virus might cause multiple sclerosis. Exhibit 18 at 3-6. This discussion does not inform the analysis of whether the homologies Dr. Steinman's BLAST searches identified are rare or common.

Sec'y of Health & Hum. Servs., 617 F.3d 1328, 1339 (Fed. Cir. 2010) (holding that a special master is not required to accept an expert's assertion simply because the expert said it). This gap in Dr. Steinman's opinion is a weakness.

c) Usefulness of the IEDB

In the next portion of Dr. Steinman's opinion, he consulted a second database, the immune epitope database (frequently abbreviated "IEDB"). He presented the sequence of amino acids from the BLAST search to see whether this sequence appears in the IEDB. Exhibit 16 at 34.

Dr. Steinman reported that the sequence of amino acids has been "studied in a T cell assay in humans." Exhibit 16 at 34, citing James.[24] Dr. Steinman does not connect this "T cell assay" to anti-NMDAR encephalitis. See id.

Dr. Lancaster wrote that consulting the IEDB "adds almost nothing." Exhibit A at 12. The reason Dr. Lancaster dismisses the IEDB is because the IEDB "is a record of every part of a protein that any person or animal has ever been shown to react against." Id. Dr. Steinman did not address this critique of the IEDB in his responsive report. See Exhibit 18.

Dr. Steinman's reliance on the IEDB tends not to increase the reliability of his opinion. See L.R. v. Sec'y of Health & Hum. Servs., No. 16-922V, 2024 WL 1912575, at *20-21 (Fed. Cl. Spec. Mstr. Mar. 28, 2024) (crediting Dr. Lancaster's opinion regarding the generality of the IEDB and stating that the special master did "not find these searches persuasive in supporting Dr. Steinman's molecular mimicry theory").

A problem with the IEDB specific to Ms. Anderson's case involving the flu vaccine causing anti-NMDA receptor encephalitis is the sparseness of information gained via the IEDB. The IEDB led Dr. Steinman to cite the 2008 article by Eddie A. James and others. But, Dr. Steinman fails to incorporate the James article into his opinion in any meaningful way. See Exhibit 16 at 34. It appears that James and colleagues determined where certain portions of an influenza B virus bind. However, the James article does not suggest that this binding would be the basis

[24] E.A. James et al., Definition of the peptide binding motif within DRB1*1401 restricted epitopes by peptide competition and structural modeling, 45 MOL. IMMUNOL. 2651 (2008); filed as Exhibit 16(13).

for an autoimmune reaction. The James article also does not suggest any adverse reaction would be manifest as anti-NMDA receptor encephalitis. Although the James article might have been one dot in a larger picture, Dr. Steinman has not persuasively connected the dots. See Le v. Sec'y of Health & Hum. Servs., No. 16-1078V, 2023 WL 3049203, at *30 (Fed. Cl. Spec. Mstr. Mar. 30, 2023) (noting that the Secretary's expert had "effectively discredited" Dr. Steinman's use of BLAST searches and the IEDB).

Overall, in the context of whether a flu vaccine can cause anti-NMDA receptor encephalitis, the evidence is lacking. Neither Ms. Anderson nor Dr. Steinman has established that molecular mimicry is a sound and reliable theory for this specific pair of antigen and disease.

3. Other Cases from the Vaccine Program

The foregoing analysis is based upon the evidence and the parties' arguments about the evidence. See 42 U.S.C. § 300aa–13(a)(1) (directing a special master to consider "the record as a whole"). Another point meriting consideration is how other judicial officers have addressed similar points, even though those resolutions are not binding. Boatmon v. Sec'y of Health & Hum. Servs., 941 F.3d 1351, 1358-59 (Fed. Cir. 2019). Decisions from special masters do not bind other special masters because, in part, different special masters can weigh even similar evidentiary records differently. Lampe v. Sec'y of Health & Hum. Servs., 219 F.3d 1357, 1368 (Fed. Cir. 2000).

The parties were encouraged to identify relevant cases involving a reasoned outcome. Order for Briefs, issued July 18, 2022, at 6. Ms. Anderson cited Al-Uffi v. Sec'y of Health & Hum. Servs., No. 13-956V, 2017 WL 1713113 (Fed. Cl. Spec. Mstr. Feb. 22, 2017). Pet'r's Br. at 23.

In Al-Uffi, the petitioner alleged the human papillomavirus vaccine caused her son to suffer anti-NMDA receptor encephalitis, which is abbreviated in Al-Uffi as "ARE." 2017 WL 1713113, at * 1. Petitioner prevailed on prong one because her "not particularly robust" evidence concerning molecular mimicry met the "relatively lenient preponderance standard that is applied in Program cases." Id. at *21. However, after Al-Uffi, non-binding but still persuasive precedents from the Court of Federal Claims have invigorated the standards of proof regarding molecular mimicry. See, e.g., Dennington, Morgan, Yalacki. Thus, Al-Uffi carries relatively little precedential force.

By way of contrast, other decisions from special masters are more consistent with appellate authorities outline above. For example, in Baron v. Sec'y of Health & Hum. Servs., No. 14-341V, 2019 WL 2273484 (Fed. Cl. Spec. Mstr. Mar. 18, 2019), the petitioners alleged that the hepatitis A and/or the flu vaccine caused their child to suffer from anti-NMDA receptor encephalitis. Id. at *1. In defending against this claim, the Secretary retained Dr. Lancaster, who has also opined in Ms. Anderson's case. See id. at *4. The special master found that the Barons had not met their burden of proof regarding Althen prong one because, in part, their expert could not link either the hepatitis A or the flu vaccine to the "very specific antibody" required in anti-NMDA receptor encephalitis. Id. at *17. This same flaw is present in Dr. Steinman's opinion.

The focus on the specific antibody is also present in another case. L.R. v. Sec'y of Health & Hum. Servs., No. 16-922V, 2024 WL 1912575, at *19-21 (Fed. Cl. Spec. Mstr. Mar. 28, 2024). The special master rejected molecular mimicry as a theory to explain how multiple vaccines might cause anti-NMDA receptor encephalitis. This conclusion is consistent with the result reached here in Ms. Anderson's case.

4. Synopsis regarding Prong One

To meet her burden regarding Althen prong one, Ms. Anderson has presented molecular mimicry as a way for the flu vaccine to cause anti-NMDAR encephalitis. There is little reliable support for claiming that the flu vaccine can cause anti-NMDA receptor encephalitis. Any such theory would need to encompass the known etiology for the condition, which involves a specific subunit of the receptor.

B. Comments on Remaining *Althen* Prongs

When petitioners fail to establish one Althen prong, additional analysis is not required. Causation-in-fact is resolved solely on the basis of Althen prong one. Any resolution of Althen prongs two and three would be entirely academic and unnecessary to decide this case.

VIII. Conclusion

Ms. Anderson and her mother deserve sympathy and admiration for their perseverance through Ms. Anderson's difficult health course. However, Ms. Anderson's case falters for two reasons. First, a preponderance of the evidence

does not support the finding that anti-NMDA receptor encephalitis is an appropriate diagnosis for her. Second, Ms. Anderson has not presented persuasive evidence that the flu vaccine was the cause of her (assumed) anti-NMDA receptor encephalitis. Thus, she is not entitled to compensation.

The Clerk's Office is instructed to enter judgment in accord with this decision unless a motion for review is filed. Information about filing a motion for review, including the deadline, can be found in the Vaccine Rules, which are available on the website for the Court of Federal Claims.

IT IS SO ORDERED.

s/Christian J. Moran
Christian J. Moran
Special Master